The Characteristics of Neuronal Stem Cells of Central Neurocytoma

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KEYWORDS

• Central neurocytoma • Histogenesis • Neuronal differentiation • Subventricular zone
• Cancer stem cell

KEY POINTS

- Angiographic findings suggest that central neurocytomas (CN) might originate from neuronal cells in the subventricular zone (SVZ) around the foramen of Monro rather than from the septum pellucidum.
- CNs have characteristics of neuronal stem cells and the potential to differentiate into mature neuronal and glial cells.
- CN-derived tumor spheres have a phenotype of transit-amplifying type C cells, which may arise from transformed transit-amplifying–type C cells that reside in the SVZ; these CN-derived tumor spheres are reminiscent of radial glial cells.
- Immunohistochemical and electrophysiologic studies show that these cells exhibit bipotential neuroglial differentiation in vitro.

INTRODUCTION

Since Hassoun and colleagues[1] first described the immunohistochemical and ultrastructural features of central neurocytoma (CN) in 1982, the number of patients diagnosed with this new entity have increased.[2] The accumulation of histopathologic, radiologic, and clinical information about CN has revealed unique characteristics. CN is a rare intraventricular neoplasm typically located in deep structures around the foramen of Monro that usually arises in young adults.[2,3] Most CNs are benign and are well-differentiated tumors with a World Health Organization Classification grade II.

Recently, CN can be diagnosed radiologically, to a certain extent, with the use of additional information such as MR spectroscopy, cerebral angiography, or conventional MR imaging.[2,3] The unique location in the subventricular zone (SVZ) provides a clue of the origin of this tumor as well as for radiologic diagnosis. However, many aspects such as the histogenesis of CN remain unknown because of its rarity. Herein, we discuss the literature on the unique characteristics and origin of CN.

THE ORIGIN OF CENTRAL NEUROCYTOMA AS SUGGESTED BY ITS ANGIOGRAPHIC CHARACTERISTICS

Traditionally, there have been 2 theories about the origin of CN. One is that, because of its attachment site, CN originates from the septum pellucidum. The other is that CN originates from the remnants of the subependymal germinal area of the lateral ventricle.[1,4,5]

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Paek and colleagues[4] analyzed the angiographic findings of 17 cases and suggested an origin of the tumors based on the angiographic findings. They reported that the blood supply to the CNs was exclusively ipsilateral through 3 routes: The lenticulostriate artery, pericallosal artery, and choroidal artery. By contrast, the CNs rarely received their blood supply from the thalamoperforating artery, which normally supplies the basal ganglia and thalamus.

Draining veins from the CNs were exclusively ipsilateral. Tortuous intraventricular veins such as the thalamostriate vein drained into the enlarged ipsilateral internal cerebral vein, and the venous angle was widened irregularly. On the contralateral side, a normal and well-demarcated thalamostriate vein drained into the internal cerebral vein of the same side, and the venous angle was smoothly widened.

Paek and colleagues[4] reported several findings that suggested that CN might not be a tumor of septal origin. The details for this conclusion are as follows. First, the feeding artery of CN originated exclusively from the ipsilateral internal carotid system and/or vertebrobasilar system. Second, the contour of the septum was preserved and deviated to the contralateral side of the CN. For this reason, the septum could be delineated from the medial margin of the CN. Third, the ipsilateral thalamostriate vein was enlarged, and the internal cerebral vein was depressed. By contrast, the sizes of the contralateral thalamostriate vein and internal cerebral vein were normal, although the venous angle was smoothly widened.

These angiographic findings suggested that the origin of CN could be inferred as the lateral ventricle. The development of CN can be explained as the result of the posterior medial and lateral choroidal arteries taking their courses above the thalamus via the velum interpositum and the floor of the lateral ventricle is compressed by the tumor itself.

In the study by Paek and colleagues, the CNs were located on the side of the lateral ventricle around the foramen of Monro between the thalamostriate vein and the internal cerebral vein. Because the venous angle between the enlarged thalamostriate vein and the internal cerebral vein was widened acutely in the ipsilateral side, the tortuously enlarged thalamostriate vein was displaced upward, whereas the internal cerebral vein was shifted downward. Moreover, MR imaging showed that the contour of the septum deviated to the contralateral ventricle from the ipsilateral ventricle where the main portion of the tumor was located, and the ventricle was enlarged.

Based on these angiographic findings, Paek and colleagues suggested that CN might originate from the neuronal cell mass of the SVZ around the foramen of Monro between the internal cerebral vein and the thalamostriate vein rather than from the septum pellucidum. They also stated that the previous claim of a septal origin of CN is understandable because, as it increases in size, a CN can grow over the origin of the tumor itself and may ultimately adhere to the surrounding ventricular walls, including the septum. Thus, the tumor can be large enough to make it difficult to verify its origin because of adhesion of the tumor to the surrounding structures.

CANCER STEM CELLS

The hypothesis that brain tumors are derived mainly from the mutation of adult cells such as astrocytes, oligodendrocytes, or neurons has been disputed by the cancer stem cell hypothesis. The cancer stem cell hypothesis proposes that a minority of transformed stem cells or progenitors acquires the ability for self-renewal, which thereby determines the tumor's behavior, including proliferation, progression, and response to therapy.[6] The persistence of germinal regions and the presence of neural stem cells (NSCs) and transit-amplifying progenitor cells in the adult brain reinforces the idea that mature neural cells are not the only possible source of tumor cells in the adult mammalian brain.[7] The presence and involvement of brain tumor stem cells in the initiation and propagation of brain tumors have been reported recently. These tumors include glioblastoma ($CD133^+$)[8]; medulloblastoma ($CD133^+$), the most frequent primary intraparenchymal neoplasm in older people[9]; and ependymoma ($CD133^+$, $nestin^+$, and brain lipid-binding protein $[BLBP]^+$), which has the highest incidence in children.[10] It has been suggested that the SVZ is a source of tumor stem cells that initiate gliomagenesis[11]; however, it is unclear which cells within the tumor mass are responsible for tumor initiation and maintenance of CN.

UNIQUE CHARACTERISTICS OF CENTRAL NEUROCYTOMA: A NEURONAL TUMOR WITH BIPOTENTIALITY

CN is a well-differentiated neuronal tumor characterized by the presence of synaptic structures, clear and dense core vesicles, and parallel microtubule structures. However, several reports have noted that CN could differentiate into both neuronal and glial cells in the in vitro culture environment.[12–15] Although the neuronal nature of the